AMENDMENTS

Amendments to the Claims

1. (Currently amended) A method of predicting or determining immunoresistance to botulinum toxin therapy in an individual, the method comprising the steps of:

a) contacting a first BoNT/A peptide and a second BoNT/A peptide with a test specimen from said individual;

~~detecting the presence or absence in said individual of antibodies immunoreactive with at least a first BoNT/A peptide and a second BoNT/A peptide;~~

wherein said first BoNT/A peptide consists essentially of ~~an amino acid sequence selected from the group consisting of~~ amino acids 785-803 of SEQ ID NO: 1, a conservative BoNT/A amino acid sequence variant thereof ~~and~~, or an immunoreactive BoNT/A amino acid sequence fragment thereof, where said conservative BoNT/A amino acid sequence variant immunoreactive with said antibodies comprises 1-4 conservative amino acid substitutions to amino acids 785-803 of SEQ ID NO: 1 and where said immunoreactive BoNT/A amino acid sequence fragment immunoreactive with said antibodies comprises at least six consecutive amino acids of 785-803 of SEQ ID NO: 1; and

wherein said second BoNT/A peptide consists essentially of ~~an amino acid sequence selected from the group consisting of~~ amino acids 981-999 of SEQ ID NO: 1, amino acids 1051-1069 of SEQ ID NO: 1, amino acids 1121-1139 of SEQ ID NO: 1, amino acids 1275-1296 of SEQ ID NO: 1, a conservative BoNT/A amino acid sequence variant thereof ~~and~~, or an immunoreactive BoNT/A amino acid sequence fragment thereof, where said conservative BoNT/A amino acid sequence variant immunoreactive with said antibodies comprises 1-4 conservative amino acid substitutions to amino acids 981-999 of SEQ ID NO: 1, 1-4 conservative amino acid substitutions to amino acids 1051-1069 of SEQ ID NO: 1, 1-4 conservative amino acid substitutions to amino acids 1121-1139 of SEQ ID NO: 1, or 1-4 conservative amino acid substitutions to amino acids 1275-1296 of SEQ ID NO: 1, and where said immunoreactive BoNT/A amino acid sequence fragment immunoreactive with said antibodies comprises at least six consecutive amino acids of 981-999 of SEQ ID

NO: 1, at least six consecutive amino acids of 1051-1069 of SEQ ID NO: 1, at least six consecutive amino acids of 1121-1139 of SEQ ID NO: 1, or at least six consecutive amino acids of 1275-1296 of SEQ ID NO: 1; and

b detecting the presence or absence in said test specimen of antibodies immunoreactive with a first BoNT/A peptide and a second BoNT/A peptide; wherein the presence of antibodies immunoreactive with ~~at least~~ said first BoNT/A peptide ~~or~~ and said second BoNT/A peptide indicates immunoresistance to a botulinum toxin therapy in an individual.

2. (Currently amended) The method of claim 1, wherein said second BoNT/A peptide consists essentially of ~~an amino acid sequence selected from the group consisting of~~ amino acids 981-999 of SEQ ID NO: 1, amino acids 1051-1069 of SEQ ID NO: 1, amino acids 1121-1139 of SEQ ID NO: 1, amino acids 1275-1296 of SEQ ID NO: 1, ~~and~~ or a conservative BoNT/A amino acid sequence variant thereof;

wherein said conservative BoNT/A amino acid sequence variant immunoreactive with said antibodies comprises 1-4 conservative amino acid substitutions to amino acids 981-999 of SEQ ID NO: 1, 1-4 conservative amino acid substitutions to amino acids 1051-1069 of SEQ ID NO: 1, 1-4 conservative amino acid substitutions to amino acids 1121-1139 of SEQ ID NO: 1, or 1-4 conservative amino acid substitutions to amino acids 1275-1296 of SEQ ID NO: 1.

3. (Currently amended) The method of claim 1, wherein said second BoNT/A peptide consists essentially of ~~an amino acid sequence selected from the group consisting of~~ amino acids 981-999 of SEQ ID NO: 1, amino acids 1051-1069 of SEQ ID NO: 1, amino acids 1121-1139 of SEQ ID NO: 1, amino acids 1275-1296 of SEQ ID NO: 1, ~~and~~ or an immunoreactive BoNT/A amino acid sequence fragment thereof;

wherein said immunoreactive BoNT/A amino acid sequence fragment immunoreactive with said antibodies comprises at least six consecutive amino acids of 981-999 of SEQ ID NO: 1, at least six consecutive amino acids of 1051-1069 of SEQ ID NO: 1, at least six consecutive amino acids of 1121-1139 of SEQ ID NO: 1, or at least six consecutive amino acids of 1275-1296 of SEQ ID NO: 1.

4. (Currently amended) The method of claim 1, wherein said second BoNT/A peptide consists essentially of ~~an amino acid sequence selected from the group consisting of~~ amino acids 981-999 of SEQ ID NO: 1, amino acids 1051-1069 of SEQ ID NO: 1, amino acids 1121-1139 of SEQ ID NO: 1, ~~and~~ or amino acids 1275-1296 of SEQ ID NO: 1.

5. (Currently amended) The method of claim 1, wherein said second BoNT/A peptide consists essentially of ~~an amino acid sequence selected from the group consisting of~~ amino acids 981-999 of SEQ ID NO:1, a conservative BoNT/A amino acid sequence variant thereof, or an immunoreactive BoNT/A amino acid sequence fragment thereof;

wherein said conservative BoNT/A amino acid sequence variant of amino acids 981-999 of SEQ ID NO:1 immunoreactive with said antibodies comprises 1-4 conservative amino acid substitutions to amino acids 981-999 of SEQ ID NO: 1; and

wherein said immunoreactive BoNT/A amino acid sequence fragment of amino acids 981-999 of SEQ ID NO:1 immunoreactive with said antibodies comprises at least six consecutive amino acids of 981-999 of SEQ ID NO: 1.

6. (Currently amended) The method of claim 1, wherein said second BoNT/A peptide consists essentially of ~~an amino acid sequence selected from the group consisting of~~ amino acids 1051-1069 of SEQ ID NO: 1, a conservative BoNT/A amino acid sequence variant thereof, or an immunoreactive BoNT/A amino acid sequence fragment thereof;

wherein said conservative BoNT/A amino acid sequence variant of amino acids 1051-1069 of SEQ ID NO:1 immunoreactive with said antibodies comprises 1-4 conservative amino acid substitutions to amino acids 1051-1069 of SEQ ID NO: 1; and

wherein said immunoreactive BoNT/A amino acid sequence fragment of amino acids 1051-1069 of SEQ ID NO:1 immunoreactive with said antibodies comprises at least six consecutive amino acids of 1051-1069 of SEQ ID NO: 1.

7. (Currently amended) The method of claim 1, wherein said second BoNT/A peptide consists essentially of ~~an amino acid sequence selected from the group consisting of~~ amino acids

1121-1139 of SEQ ID NO: 1, a conservative BoNT/A amino acid sequence variant thereof, or an immunoreactive BoNT/A amino acid sequence fragment thereof;

wherein said conservative BoNT/A amino acid sequence variant of amino acids 1121-1139 of SEQ ID NO:1 immunoreactive with said antibodies comprises 1-4 conservative amino acid substitutions to amino acids 1121-1139 of SEQ ID NO: 1; and

wherein said immunoreactive BoNT/A amino acid sequence fragment of amino acids 1121-1139 of SEQ ID NO:1 immunoreactive with said antibodies comprises at least six consecutive amino acids of 1121-1139 of SEQ ID NO: 1.

8. (Currently amended) The method of claim 1, wherein said second BoNT/A peptide consists essentially of ~~an amino acid sequence selected from the group consisting of~~ amino acids 1275-1296 of SEQ ID NO: 1, a conservative BoNT/A amino acid sequence variant thereof, or an immunoreactive BoNT/A amino acid sequence fragment thereof;

wherein said conservative BoNT/A amino acid sequence variant of amino acids 1275-1296 of SEQ ID NO:1 immunoreactive with said antibodies comprises 1-4 conservative amino acid substitutions to amino acids 1275-1296 of SEQ ID NO: 1; and

wherein said immunoreactive BoNT/A amino acid sequence fragment of amino acids 1275-1296 of SEQ ID NO:1 immunoreactive with said antibodies comprises at least six consecutive amino acids of 1275-1296 of SEQ ID NO: 1.

9. (Currently amended) The method of claim 1, wherein said first BoNT/A peptide consists essentially of ~~an amino acid sequence selected from the group consisting of~~ amino acids 785-803 of SEQ ID NO: 1, or a conservative BoNT/A amino acid sequence variant thereof;

wherein said conservative BoNT/A amino acid sequence variant immunoreactive with said antibodies comprises 1-4 conservative amino acid substitutions to amino acids 785-803 of SEQ ID NO: 1.

10. (Currently amended) The method of claim 1, wherein ~~two of~~ said ~~additional~~ first BoNT/A peptide consists essentially of ~~an amino acid sequence selected from the group consisting of~~ amino acids 785-803 of SEQ ID NO: 1, or an immunoreactive BoNT/A amino acid sequence fragment thereof;

wherein said immunoreactive BoNT/A amino acid sequence fragment immunoreactive with said antibodies comprises at least six consecutive amino acids of 785-803 of SEQ ID NO: 1.

11. (Currently amended) The method of claim 1, wherein ~~two of~~ said ~~additional~~ first BoNT/A peptide consists essentially of ~~an amino acid sequence selected from the group consisting of~~ amino acids 785-803 of SEQ ID NO: 1.

12. (Currently amended) A method of predicting or determining immunoresistance to botulinum toxin therapy in an individual, the method comprising the steps of:

a) contacting a BoNT/A peptide with a test specimen from said individual, ~~detecting the presence or absence in said individual of antibodies immunoreactive with at least a BoNT/A peptide,~~ said BoNT/A peptide ~~consists~~ consisting essentially of ~~an amino acid sequence selected from the group consisting of~~ amino acids 785-803 of SEQ ID NO: 1, a conservative BoNT/A amino acid sequence variant thereof ~~and~~, or an immunoreactive BoNT/A amino acid sequence fragment thereof;

wherein said conservative BoNT/A amino acid sequence variant of amino acids 785-803 of SEQ ID NO:1 immunoreactive with said antibodies comprises 1-4 conservative amino acid substitutions to amino acids 785-803 of SEQ ID NO: 1; and

wherein said immunoreactive BoNT/A amino acid sequence fragment of amino acids 785-803 of SEQ ID NO:1 immunoreactive with said antibodies comprises at least six consecutive amino acids of 785-803 of SEQ ID NO: 1; and

b detecting the presence or absence in said test specimen of antibodies immunoreactive with said BoNT/A peptide; wherein the presence of antibodies immunoreactive with said BoNT/A peptide indicates immunoresistance to a botulinum toxin therapy in an individual.

13. (Previously presented) The method of claim 12, wherein said BoNT/A peptide consists essentially of amino acids 785-803 of SEQ ID NO: 1.

14. (Currently amended) The method of claim 1, comprising selectively ~~determining~~ detecting the presence or absence in said individual of IgG antibodies immunoreactive with each of said immunoreactive first or second BoNT/A peptide.

15. (Currently amended) The method of claim 1 ~~or 12~~, wherein the presence or absence of antibodies immunoreactive with each of said immunoreactive first or second BoNT/A peptide is ~~determined~~ detected using an enzyme-linked immunosorbent assay.

16. (Currently amended) The method of claim 1 ~~or 12~~, wherein the presence or absence of antibodies immunoreactive with each of said immunoreactive first or second BoNT/A peptide is ~~determined~~ detected using a radioimmunoassay.

17. (Previously presented) The method of claim 1 or 12, wherein said botulinum toxin therapy is BoNT/A therapy.

18-30 (Cancelled).

31. (Currently amended) A method of producing antibodies that neutralize BoNT/A in an individual, the method comprising the step of administering to said individual an immune response inducing composition comprising:

    a) an adjuvant;

    b) a BoNT/A peptide having a length of at most 60 amino acids and comprising amino acids 785-803 of SEQ ID NO: 1 or an immunoreactive BoNT/A amino acid sequence fragment thereof;

wherein said amino acids 785-803 of SEQ ID NO: 1 and said immunoreactive BoNT/A amino acid sequence fragment thereof stimulate an immune response capable of producing a neutralizing anti-BoNT/A antibody; and

wherein said immunoreactive BoNT/A amino acid sequence fragment stimulating an immune response comprises at least ~~six~~ eight consecutive amino acids of 785-803 of SEQ ID NO: 1; and

c) at least one additional BoNT/A peptide, said additional BoNT/A peptide having a length of at most 60 amino acids and comprising ~~an amino acid sequence selected from the group consisting of~~ amino acids 981-999 of SEQ ID NO: 1, amino acids 1051-1069 of SEQ ID NO: 1, amino acids 1121-1139 of SEQ ID NO: 1, amino acids 1275-1296 of SEQ ID NO: 1 ~~and~~, or an immunoreactive BoNT/A amino acid sequence fragment thereof;

wherein said amino acids 981-999 of SEQ ID NO: 1, amino acids 1051-1069 of SEQ ID NO: 1, amino acids 1121-1139 of SEQ ID NO: 1, amino acids 1275-1296 of SEQ ID NO: 1 and an immunoreactive BoNT/A amino acid sequence fragment thereof stimulate an immune response capable of producing a neutralizing anti-BoNT/A antibody; and

wherein said immunoreactive BoNT/A amino acid sequence fragment stimulating an immune response comprises at least ~~six~~ eight consecutive amino acids of 981-999 of SEQ ID NO: 1, at least ~~six~~ eight consecutive amino acids of 1051-1069 of SEQ ID NO: 1, at least ~~six~~ eight consecutive amino acids of 1121-1139 of SEQ ID NO: 1 or at least ~~six~~ eight consecutive amino acids of 1275-1296 of SEQ ID NO: 1.

32. (Currently amended) The method of claim 31, wherein said additional BoNT/A peptide comprises ~~an amino acid sequence selected from the group consisting of~~ amino acids 981-999 of SEQ ID NO: 1, amino acids 1051-1069 of SEQ ID NO: 1, amino acids 1121-1139 of SEQ ID NO: 1, ~~and~~ or amino acids 1275-1296 of SEQ ID NO: 1.

33. (Currently amended) The method of claim 31, wherein said additional BoNT/A peptide includes said additional BoNT/A peptide comprising amino acids 981-999 of SEQ ID NO: 1 or an immunoreactive BoNT/A amino acid sequence fragment thereof;

wherein said immunoreactive BoNT/A amino acid sequence fragment of amino acids 981-999 of SEQ ID NO:1 stimulating an immune response comprises at least ~~six~~ eight consecutive amino acids of 981-999 of SEQ ID NO: 1.

34. (Currently amended) The method of claim 31, wherein said additional BoNT/A peptide includes said additional BoNT/A peptide comprising amino acids 1051-1069 of SEQ ID NO: 1 or an immunoreactive BoNT/A amino acid sequence fragment thereof;

wherein said immunoreactive BoNT/A amino acid sequence fragment of amino acids 1051-1069 of SEQ ID NO:1 stimulating an immune response comprises at least ~~six~~ eight consecutive amino acids of 1051-1069 of SEQ ID NO: 1.

35. (Currently amended) The method of claim 31, wherein said additional BoNT/A peptide includes said additional BoNT/A peptide comprising amino acids 1275-1296 of SEQ ID NO: 1 or an immunoreactive BoNT/A amino acid sequence fragment thereof;

wherein said immunoreactive BoNT/A amino acid sequence fragment of amino acids 1275-1296 of SEQ ID NO:1 stimulating an immune response comprises at least ~~six~~ eight consecutive amino acids of 1275-1296 of SEQ ID NO: 1.

36. (Previously presented) The method of claim 31, wherein said additional BoNT/A peptide includes said additional BoNT/A peptide comprising amino acids 1051-1069 of SEQ ID NO: 1 and said additional BoNT/A peptide comprising amino acids 1121-1139 of SEQ ID NO: 1.

37. (Previously presented) The method of claim 31, wherein said additional BoNT/A peptide includes said additional BoNT/A peptide comprising amino acids 981-999 of SEQ ID NO: 1 and said additional BoNT/A peptide comprising amino acids1051-1069 of SEQ ID NO: 1.

38. (Previously presented) The method of claim 31, wherein said additional BoNT/A peptide includes said additional BoNT/A peptide comprising amino acids 981-999 of SEQ ID NO: 1 and said additional BoNT/A peptide comprising amino acids 1121-1139 of SEQ ID NO: 1.

39. (Previously presented) The method of claim 31, wherein said additional BoNT/A peptide includes said additional BoNT/A peptide comprising amino acids 981-999 of SEQ ID NO: 1 and said additional BoNT/A peptide comprising amino acids 1275-1296 of SEQ ID NO: 1.

40. (Previously presented) The method of claim 31, wherein said additional BoNT/A peptide includes said additional BoNT/A peptide comprising amino acids 981-999 of SEQ ID NO: 1, said additional BoNT/A peptide comprising amino acids 1051-1069 of SEQ ID NO: 1 and said additional BoNT/A peptide comprising amino acids 1121-1139 of SEQ ID NO: 1.

41. (Previously presented) The method of claim 31, wherein said additional BoNT/A peptide includes said additional BoNT/A peptide comprising amino acids 981-999 of SEQ ID NO: 1, said additional BoNT/A peptide comprising amino acids 1121-1139 of SEQ ID NO: 1 and said additional BoNT/A peptide comprising amino acids 1275-1296 of SEQ ID NO: 1.

42. (Previously presented) The method of claim 31, wherein said additional BoNT/A peptide includes said additional BoNT/A peptide comprising amino acids 1051-1069 of SEQ ID NO: 1, said additional BoNT/A peptide comprising amino acids 1121-1139 of SEQ ID NO: 1 and said additional BoNT/A peptide comprising amino acids 1275-1296 of SEQ ID NO: 1.

43. (Previously presented) The method of claim 31, wherein said additional BoNT/A peptide includes said additional BoNT/A peptide comprising amino acids 981-999 of SEQ ID NO: 1, said additional BoNT/A peptide comprising amino acids 1051-1069 of SEQ ID NO: 1, said additional BoNT/A peptide comprising amino acids 1121-1139 of SEQ ID NO: 1 and said additional BoNT/A peptide comprising amino acids 1275-1296 of SEQ ID NO: 1.

44-47. (Cancelled).

48. (Currently amended) A method of predicting or determining immunoresistance to botulinum toxin therapy in an individual, the method comprising the steps of:

(a) ~~determining~~ detecting the level of IgG antibodies immunoreactive with at least one BoNT/A peptide, said BoNT/A peptide having a length of at most 60 amino acids and comprising ~~an amino acid sequence selected from the group consisting of~~ amino acids 785-803 of

SEQ ID NO: 1, amino acids 981-999 of SEQ ID NO: 1, amino acids 1051-1069 of SEQ ID NO: 1, amino acids 1121-1139 of SEQ ID NO: 1, amino acids 1275-1296 of SEQ ID NO: 1, a conservative BoNT/A amino acid sequence variant thereof ~~and~~, or an immunoreactive BoNT/A amino acid sequence fragment thereof;

wherein said IgG antibodies immunoreact with amino acids 785-803 of SEQ ID NO: 1, amino acids 981-999 of SEQ ID NO: 1, amino acids 1051-1069 of SEQ ID NO: 1, amino acids 1121-1139 of SEQ ID NO: 1, amino acids 1275-1296 of SEQ ID NO: 1, a conservative BoNT/A amino acid sequence variant thereof, or an immunoreactive BoNT/A amino acid sequence fragment thereof;

wherein said conservative BoNT/A amino acid sequence variant immunoreactive with said IgG antibodies comprises 1-4 conservative amino acid substitutions to amino acids 785-803 of SEQ ID NO: 1, 1-4 conservative amino acid substitutions to amino acids 981-999 of SEQ ID NO: 1, 1-4 conservative amino acid substitutions to amino acids 1051-1069 of SEQ ID NO: 1, 1-4 conservative amino acid substitutions to amino acids 1121-1139 of SEQ ID NO: 1, or 1-4 conservative amino acid substitutions to amino acids 1275-1296 of SEQ ID NO: 1; and

wherein said immunoreactive BoNT/A amino acid sequence fragment immunoreactive with said IgG antibodies comprises at least six consecutive amino acids of 785-803 of SEQ ID NO: 1, at least six consecutive amino acids of 981-999 of SEQ ID NO: 1, at least six consecutive amino acids of 1051-1069 of SEQ ID NO: 1, at least six consecutive amino acids of 1121-1139 of SEQ ID NO: 1, or at least six consecutive amino acids of 1275-1296 of SEQ ID NO: 1; and

(b) comparing said level of IgG antibodies to a control level of IgG antibodies;

wherein an increase in said level of IgG antibodies in said individual as compared to said control level indicates immunoresistance to said botulinum toxin therapy.

49. (Previously presented) The method of claim 48, wherein said increase is at least a 5-fold increase.

50. (Previously presented) The method of claim 48, wherein said increase is at least a 10-fold increase.

51. (Currently amended) The method of claim 48, wherein said control level of IgG antibodies is ~~determined~~ detected in an individual who has not been treated with botulinum toxin therapy.

52. (Currently amended) The method of claim 48, wherein said control level of IgG antibodies is ~~determined~~ detected in an individual who is responsive to said botulinum toxin therapy.

53. (Previously presented) The method of claim 48, wherein said botulinum toxin therapy is a BoNT/A therapy.

54. (Currently amended) A method of predicting or determining immunoresistance to botulinum toxin therapy in an individual, the method comprising the steps of:

a) contacting a BoNT/A peptide of SEQ ID NO: 1 having a length of at most 60 amino acids with a test specimen from said individual, said BoNT/A peptide comprising ~~an amino acid sequence selected from the group consisting of~~ amino acids 785-803 of SEQ ID NO: 1, a conservative BoNT/A amino acid sequence variant thereof ~~and~~, or an immunoreactive BoNT/A amino acid sequence fragment thereof;

wherein said conservative BoNT/A amino acid sequence variant of amino acids 785-803 of SEQ ID NO:1 immunoreactive with said antibodies comprises 1-4 conservative amino acid substitutions to amino acids 785-803 of SEQ ID NO: 1;

wherein said immunoreactive BoNT/A amino acid sequence fragment of amino acids 785-803 of SEQ ID NO:1 immunoreactive with said antibodies comprises at least six consecutive amino acids of 785-803 of SEQ ID NO: 1; and

b) detecting the presence or absence of antibodies immunoreactive with said BoNT/A peptide;

wherein said antibodies immunoreact with said amino acid sequence from said BoNT/A peptide, said amino acid sequence comprising amino acids 785-803 of SEQ ID NO: 1, a conservative BoNT/A amino acid sequence variant thereof, or an immunoreactive BoNT/A amino acid sequence fragment thereof; and

wherein the presence of antibodies immunoreactive with said BoNT/A peptide indicates immunoresistance to a botulinum toxin therapy.

55. (Currently amended) The method of claim 54, further comprising at least one additional BoNT/A peptide of SEQ ID NO: 1 in step (a), said additional BoNT/A peptides having a length of at most 60 amino acids and comprising ~~an amino acid sequence selected from the group consisting of~~ amino acids 981-999 of SEQ ID NO: 1, amino acids 1051-1069 of SEQ ID NO: 1 and amino acids 1121-1139 of SEQ ID NO: 1, amino acids 1275-1296 of SEQ ID NO: 1, a conservative BoNT/A amino acid sequence variant thereof ~~and~~, or an immunoreactive BoNT/A amino acid sequence fragment thereof;

wherein said conservative BoNT/A amino acid sequence variant immunoreactive with said antibodies comprises 1-4 conservative amino acid substitutions to amino acids 981-999 of SEQ ID NO: 1, 1-4 conservative amino acid substitutions to amino acids 1051-1069 of SEQ ID NO: 1, 1-4 conservative amino acid substitutions to amino acids 1121-1139 of SEQ ID NO: 1, or 1-4 conservative amino acid substitutions to amino acids 1275-1296 of SEQ ID NO: 1;

wherein said immunoreactive BoNT/A amino acid sequence fragment immunoreactive with said antibodies comprises at least six consecutive amino acids of 981-999 of SEQ ID NO: 1, at least six consecutive amino acids of 1051-1069 of SEQ ID NO: 1, at least six consecutive amino acids of 1121-1139 of SEQ ID NO: 1, or at least six consecutive amino acids of 1275-1296 of SEQ ID NO: 1;

wherein said antibodies of step (b) immunoreact with said amino acid sequence of said additional BoNT/A peptides, said amino acid sequence selected from the group consisting of amino acids 981-999 of SEQ ID NO: 1, amino acids 1051-1069 of SEQ ID NO: 1 and amino acids 1121-1139 of SEQ ID NO: 1, amino acids 1275-1296 of SEQ ID NO: 1, a conservative

BoNT/A amino acid sequence variant thereof, or an immunoreactive BoNT/A amino acid sequence fragment thereof; and

wherein the presence of antibodies immunoreactive with at least one of said additional BoNT/A peptides indicates immunoresistance to a botulinum toxin therapy.

56. (Previously presented) The method of claim 54, wherein said BoNT/A peptide has a length of at most 40 amino acids.

57. (Previously presented) The method of claim 55, wherein said additional BoNT/A peptides have a length of at most 40 amino acids.

58. (Currently amended) The method of claim 55, wherein said additional BoNT/A peptide comprises ~~an amino acid sequence selected from the group consisting of~~ amino acids 981-999 of SEQ ID NO: 1, a conservative BoNT/A amino acid sequence variant thereof ~~and~~, or an immunoreactive BoNT/A amino acid sequence fragment thereof;

wherein said conservative BoNT/A amino acid sequence variant of amino acids 981-999 of SEQ ID NO:1 immunoreactive with said antibodies comprises 1-4 conservative amino acid substitutions to amino acids 981-999 of SEQ ID NO: 1; and

wherein said immunoreactive BoNT/A amino acid sequence fragment of amino acids 981-999 of SEQ ID NO:1 immunoreactive with said antibodies comprises at least six consecutive amino acids of 981-999 of SEQ ID NO: 1.

59. (Currently amended) The method of claim 55, wherein said additional BoNT/A peptide comprises ~~an amino acid sequence selected from the group consisting of~~ amino acids 1051-1069 of SEQ ID NO: 1, a conservative BoNT/A amino acid sequence variant thereof ~~and~~, or an immunoreactive BoNT/A amino acid sequence fragment thereof;

wherein said conservative BoNT/A amino acid sequence variant of amino acids 1051-1069 of SEQ ID NO:1 immunoreactive with said antibodies comprises 1-4 conservative amino acid substitutions to amino acids 1051-1069 of SEQ ID NO: 1; and

wherein said immunoreactive BoNT/A amino acid sequence fragment of amino acids 1051-1069 of SEQ ID NO:1 immunoreactive with said antibodies comprises at least six consecutive amino acids of 1051-1069 of SEQ ID NO: 1.

60. (Currently amended) The method of claim 55, wherein said additional BoNT/A peptide comprises ~~an amino acid sequence selected from the group consisting of~~ amino acids 1121-1139 of SEQ ID NO: 1, a conservative BoNT/A amino acid sequence variant thereof ~~and~~, or an immunoreactive BoNT/A amino acid sequence fragment thereof;

wherein said conservative BoNT/A amino acid sequence variant of amino acids 1121-1139 of SEQ ID NO:1 immunoreactive with said antibodies comprises 1-4 conservative amino acid substitutions to amino acids 1121-1139 of SEQ ID NO: 1; and

wherein said immunoreactive BoNT/A amino acid sequence fragment of amino acids 1121-1139 of SEQ ID NO:1 immunoreactive with said antibodies comprises at least six consecutive amino acids of 1121-1139 of SEQ ID NO: 1.

61. (Currently amended) The method of claim 55, wherein said additional BoNT/A peptide comprises ~~an amino acid sequence selected from the group consisting of~~ amino acids 1275-1296 of SEQ ID NO: 1, a conservative BoNT/A amino acid sequence variant thereof ~~and~~, or an immunoreactive BoNT/A amino acid sequence fragment thereof;

wherein said conservative BoNT/A amino acid sequence variant of amino acids 1275-1296 of SEQ ID NO:1 immunoreactive with said antibodies comprises 1-4 conservative amino acid substitutions to amino acids 1275-1296 of SEQ ID NO: 1; and

wherein said immunoreactive BoNT/A amino acid sequence fragment of amino acids 1275-1296 of SEQ ID NO:1 immunoreactive with said antibodies comprises at least six consecutive amino acids of 1275-1296 of SEQ ID NO: 1.

62. (Canceled)

63. (Previously presented) The method of claim 54 or 55, comprising selectively determining the presence or absence of IgG antibody component from said antibodies immunoreactive with said amino acid sequences.

64-66. (Canceled)

67. (Previously presented) The method of claim 55, wherein the presence or absence of antibodies immunoreactive with two or more of said additional amino acid sequences is determined.

68. (Previously presented) The method of claim 55, wherein the presence or absence of antibodies immunoreactive with three or more of said additional amino acid sequences is determined.

69. (Previously presented) The method of claim 55, wherein the presence or absence of antibodies immunoreactive with four of said additional amino acid sequences is determined.

70. (Previously presented) The method of claim 54, wherein said BoNT/A peptide is immobilized on a solid support.

71. (Previously presented) The method of claim 55, wherein said additional BoNT/A peptides are immobilized on a solid support.

72. (Previously presented) The method of claim 54 or 55, wherein the presence or absence of said immunoreactive antibodies is determined using a radioimmunoassay or an enzyme-linked immunosorbent assay.

73. (Previously presented) The method of claim 54 or 55, wherein said botulinum toxin therapy is a BoNT/A therapy.

74-113. (Canceled)

114. (Currently amended) An immune response inducing composition, comprising an adjuvant and a BoNT/A peptide of SEQ ID NO: 1, said BoNT/A peptide having a length of at most 60 amino acids and comprising ~~an amino acid sequence selected from the group consisting of~~ amino acids 785-794 of SEQ ID NO: 1 ~~and~~ or an immunoreactive BoNT/A amino acid sequence fragment thereof;

wherein said amino acids 785-794 of SEQ ID NO: 1 and said immunoreactive BoNT/A amino acid sequence fragment thereof stimulate an immune response capable of producing a neutralizing anti-BoNT/A antibody; and

wherein said immunoreactive BoNT/A amino acid sequence fragment of amino acids 785-794 of SEQ ID NO:1 stimulating an immune response comprises at least ~~six~~ eight consecutive amino acids of 785-794 of SEQ ID NO: 1.

115. (Currently amended) The immune response inducing composition of claim 114, further comprising an additional BoNT/A peptide of SEQ ID NO: 1, said additional BoNT/A peptide having a length of at most 60 amino acids and comprising ~~an amino acid sequence selected from the group consisting of~~ amino acids 981-999 of SEQ ID NO: 1, amino acids 1051-1069 of SEQ ID NO: 1, amino acids 1121-1139 of SEQ ID NO: 1, amino acids 1275-1296 of SEQ ID NO: 1 ~~and~~, or an immunoreactive BoNT/A amino acid sequence fragment thereof;

wherein said amino acids 981-999 of SEQ ID NO: 1, amino acids 1051-1069 of SEQ ID NO: 1, amino acids 1121-1139 of SEQ ID NO: 1, amino acids 1275-1296 of SEQ ID NO: 1 and, an immunoreactive BoNT/A amino acid sequence fragment thereof stimulate an immune response capable of producing a neutralizing anti-BoNT/A antibody; and

wherein said immunoreactive BoNT/A amino acid sequence fragment stimulating an immune response comprises at least ~~six~~ eight consecutive amino acids of 785-803 of SEQ ID NO: 1, at least ~~six~~ eight consecutive amino acids of 981-999 of SEQ ID NO: 1, at least ~~six~~ eight consecutive amino acids of 1051-1069 of SEQ ID NO: 1, at least ~~six~~ eight consecutive amino acids of 1121-1139 of SEQ ID NO: 1, or at least ~~six~~ eight consecutive amino acids of 1275-1296 of SEQ ID NO: 1.

116. (Previously presented) The composition of claim 114, wherein said BoNT/A peptide has a length of at most 40 amino acids.

117. (Previously presented) The composition of claim 115, wherein said additional BoNT/A peptides have a length of at most 40 amino acids.

118. (Currently amended) The composition of claim 115, wherein said additional BoNT/A peptide comprises ~~an amino acid sequence selected from the group consisting of~~ amino acids 981-999 of SEQ ID NO: 1 ~~and~~ or an immunoreactive BoNT/A amino acid sequence fragment thereof;

wherein said immunoreactive BoNT/A amino acid sequence fragment of amino acids 981-999 of SEQ ID NO:1 stimulating an immune response comprises at least ~~six~~ eight consecutive amino acids of 981-999 of SEQ ID NO: 1.

119. (Currently amended) The composition of claim 115, wherein said additional BoNT/A peptide comprises ~~an amino acid sequence selected from the group consisting of~~ amino acids 1051-1069 of SEQ ID NO: 1 ~~and~~ or an immunoreactive BoNT/A amino acid sequence fragment thereof;

wherein said immunoreactive BoNT/A amino acid sequence fragment of amino acids 1051-1069 of SEQ ID NO:1 stimulating an immune response comprises at least ~~six~~ eight consecutive amino acids of 1051-1069 of SEQ ID NO: 1.

120. (Currently amended) The composition of claim 115, wherein said additional BoNT/A peptide comprises ~~an amino acid sequence selected from the group consisting of~~ amino acids 1121-1139 of SEQ ID NO: 1 ~~and~~ or an immunoreactive BoNT/A amino acid sequence fragment thereof;

wherein said immunoreactive BoNT/A amino acid sequence fragment of amino acids 1121-1139 of SEQ ID NO:1 stimulating an immune response comprises at least ~~six~~ eight consecutive amino acids of 1121-1139 of SEQ ID NO: 1.

121. (Currently amended) The composition of claim 115, wherein said additional BoNT/A peptide comprises ~~an amino acid sequence selected from the group consisting of~~ amino acids 1275-1296 of SEQ ID NO: 1 ~~and~~ or an immunoreactive BoNT/A amino acid sequence fragment thereof;

wherein said immunoreactive BoNT/A amino acid sequence fragment of amino acids 1275-1296 of SEQ ID NO:1 stimulating an immune response comprises at least ~~six~~ eight consecutive amino acids of 1275-1296 of SEQ ID NO: 1.

122. (Canceled)

123. (Currently amended) A method of preparing an anti-BoNT/A antibody, the method comprising the steps of:

(a) administering to an animal a composition comprising an adjuvant and a BoNT/A peptide of SEQ ID NO: 1 having a length of at most 30 amino acids;

wherein said BoNT/A peptide comprises ~~an amino acid sequence selected from the group consisting of~~ amino acids 491-509 of SEQ ID NO: 1, amino acids 519-537 of SEQ ID NO: 1, amino acids 533-551 of SEQ ID NO: 1, amino acids 547-565 of SEQ ID NO: 1, amino acids 589-607 of SEQ ID NO: 1, amino acids 631-649 of SEQ ID NO: 1, amino acids 659-677 of SEQ ID NO: 1, amino acids 673-691 of SEQ ID NO: 1, 715-733 of SEQ ID NO: 1, amino acids 743-761 of SEQ ID NO: 1, amino acids 771-789 of SEQ ID NO: 1, amino acids 785-803 of SEQ ID NO: 1, amino acids 813-831 of SEQ ID NO: 1, amino acids 827-845 of SEQ ID NO: 1 ~~and~~, or an immunogenic BoNT/A amino acid sequence fragment thereof;

wherein an immunogenic response is produced by amino acids 491-509 of SEQ ID NO: 1, amino acids 519-537 of SEQ ID NO: 1, amino acids 533-551 of SEQ ID NO: 1, amino acids 547-565 of SEQ ID NO: 1, amino acids 589-607 of SEQ ID NO: 1, amino acids 631-649 of SEQ ID NO: 1, amino acids 659-677 of SEQ ID NO: 1, amino acids 673-691 of SEQ ID NO: 1, 715-733 of SEQ ID NO: 1, amino acids 743-761 of SEQ ID NO: 1, amino acids 771-789 of SEQ ID NO: 1, amino acids 785-803 of SEQ ID NO: 1,

amino acids 813-831 of SEQ ID NO: 1, amino acids 827-845 of SEQ ID NO: 1, or an immunogenic BoNT/A amino acid sequence fragment thereof; and

wherein said immunogenic BoNT/A amino acid sequence stimulating an immunogenic response comprises at least ~~six~~ eight consecutive amino acids of 491-509 of SEQ ID NO: 1, at least ~~six~~ eight consecutive amino acids of 519-537 of SEQ ID NO: 1, at least ~~six~~ eight consecutive amino acids of 533-551 of SEQ ID NO: 1, at least ~~six~~ eight consecutive amino acids of 547-565 of SEQ ID NO: 1, at least ~~six~~ eight consecutive amino acids of 589-607 of SEQ ID NO: 1, at least ~~six~~ eight consecutive amino acids of 631-649 of SEQ ID NO: 1, at least ~~six~~ eight consecutive amino acids of 659-677 of SEQ ID NO: 1, at least ~~six~~ eight consecutive amino acids of 673-691 of SEQ ID NO: 1, at least ~~six~~ eight consecutive amino acids of 715-733 of SEQ ID NO: 1, at least ~~six~~ eight consecutive amino acids of 743-761 of SEQ ID NO: 1, at least ~~six~~ eight consecutive amino acids of 771-789 of SEQ ID NO: 1, at least ~~six~~ eight consecutive amino acids of 785-803 of SEQ ID NO: 1, at least ~~six~~ eight consecutive amino acids of 813-831 of SEQ ID NO: 1, or at least ~~six~~ eight consecutive amino acids of 827-845 of SEQ ID NO: 1;

(b) collecting from said animal a sample containing an antibody or antibody-producing cell; and

(c) processing said sample to isolate said anti-BoNT/A antibody.

124. (Currently amended) The method of claim 123, wherein said BoNT/A peptide comprises ~~an amino acid sequence selected from the group consisting of~~ amino acids 547-565 of SEQ ID NO: 1, amino acids 589-607 of SEQ ID NO: 1, amino acids 659-677 of SEQ ID NO: 1, amino acids 743-761 of SEQ ID NO: 1, amino acids 785-803 of SEQ ID NO: 1 ~~and~~, or an immunogenic BoNT/A amino acid sequence fragment thereof;

wherein said immunogenic BoNT/A amino acid sequence stimulating an immunogenic response comprises at least ~~six~~ eight consecutive amino acids of 547-565 of SEQ ID NO: 1, at least ~~six~~ eight consecutive amino acids of 589-607 of SEQ ID NO: 1, at least ~~six~~ eight consecutive amino acids of 659-677 of SEQ ID NO: 1, at least ~~six~~ eight consecutive amino

acids of 743-761 of SEQ ID NO: 1, or at least ~~six~~ eight consecutive amino acids of 785-803 of SEQ ID NO: 1.

125. (Previously presented) The method of claim 123, wherein said BoNT/A peptide has a length of at most 25 amino acids.

126. (Previously presented) The method of claim 123, wherein said BoNT/A peptide has a length of at most 20 amino acids.

127. (Currently amended) The method of claim 123, wherein said BoNT/A peptide comprises ~~an amino acid sequence selected from the group consisting of~~ amino acids 547-565 of SEQ ID NO: 1, amino acids 785-803 of SEQ ID NO: 1 ~~and~~, or a immunogenic BoNT/A amino acid sequence fragment thereof;

wherein said immunogenic BoNT/A amino acid sequence stimulating an immunogenic response comprises at least ~~six~~ eight consecutive amino acids of 547-565 of SEQ ID NO: 1, or at least ~~six~~ eight consecutive amino acids of 785-803 of SEQ ID NO: 1.

128. (Currently amended) The method of claim 123, wherein said BoNT/A peptide comprises ~~an amino acid sequence selected from the group consisting of~~ amino acids 449-467 of SEQ ID NO: 1, amino acids 491-509 of SEQ ID NO: 1, amino acids 519-537 of SEQ ID NO: 1, amino acids 533-551 of SEQ ID NO: 1, amino acids 547-565 of SEQ ID NO: 1, amino acids 589-607 of SEQ ID NO: 1, amino acids 631-649 of SEQ ID NO: 1, amino acids 659-677 of SEQ ID NO: 1, amino acids 673-691 of SEQ ID NO: 1, 715-733 of SEQ ID NO: 1, amino acids 743-761 of SEQ ID NO: 1, amino acids 771-789 of SEQ ID NO: 1, amino acids 785-803 of SEQ ID NO: 1, amino acids 813-831 of SEQ ID NO: 1 ~~and~~, or amino acids 827-845 of SEQ ID NO: 1.

129. (Currently amended) The method of claim 123, wherein said BoNT/A peptide comprises ~~an amino acid sequence selected from the group consisting of~~ amino acids 547-565 of SEQ ID NO: 1, amino acids 589-607 of SEQ ID NO: 1, amino acids 659-677 of SEQ ID NO: 1, amino acids 743-761 of SEQ ID NO: 1 ~~and~~, or amino acids 785-803 of SEQ ID NO: 1.

130. (Currently amended) The method of claim 123, wherein said BoNT/A peptide comprises ~~consists of an amino acid sequence selected from the group consisting of~~ amino acids 547-565 of SEQ ID NO: 1 ~~and~~ or amino acids 785-803 of SEQ ID NO: 1.

131. (Currently amended) The method of claim 123, wherein said BoNT/A peptide comprises amino acids 785-803 of SEQ ID NO: 1[[,]] or immunogenic BoNT/A amino acid sequence fragment thereof;

wherein said immunogenic BoNT/A amino acid sequence fragment of amino acids 785-803 of SEQ ID NO: 1 stimulating an immunogenic response comprises at least ~~six~~ eight consecutive amino acids of 785-803 of SEQ ID NO: 1.

132. (Original) The method of claim 123, wherein said antibody is polyclonal.

133. (Original) The method of claim 123, wherein said antibody is monoclonal.

134-135. (Cancelled)

136. (Currently amended) The method of claim 12, further comprising detecting the presence or absence in said individual of antibodies immunoreactive with at least one additional BoNT/A peptide of SEQ ID NO: 1, said additional BoNT/A peptide consisting essentially of ~~an amino acid sequence selected from the group consisting of~~ amino acids 981-999 of SEQ ID NO: 1, amino acids 1051-1069 of SEQ ID NO: 1, ~~and~~ amino acids 1121-1139 of SEQ ID NO: 1, amino acids 1275-1296 of SEQ ID NO: 1, a conservative BoNT/A amino acid sequence variant thereof ~~and~~, or an immunoreactive BoNT/A amino acid sequence fragment thereof;

wherein said conservative BoNT/A amino acid sequence variant immunoreactive with said antibodies comprises 1-4 conservative amino acid substitutions to amino acids 981-999 of SEQ ID NO: 1, 1-4 conservative amino acid substitutions to amino acids 1051-1069 of SEQ ID NO: 1, 1-4 conservative amino acid substitutions to amino acids 1121-1139 of SEQ ID NO: 1, or 1-4 conservative amino acid substitutions to amino acids 1275-1296 of SEQ ID NO: 1;

wherein said immunoreactive BoNT/A amino acid sequence fragment immunoreactive with said antibodies comprises at least ~~six~~ eight consecutive amino acids of 981-999 of SEQ ID NO: 1, at least ~~six~~ eight consecutive amino acids of 1051-1069 of SEQ ID NO: 1, at least ~~six~~ eight consecutive amino acids of 1121-1139 of SEQ ID NO: 1, or at least ~~six~~ eight consecutive amino acids of 1275-1296 of SEQ ID NO: 1;

wherein the presence of antibodies immunoreactive with at least one of said additional BoNT/A peptides indicates immunoresistance to a botulinum toxin therapy.

137. (New) The method of claim 12, comprising selectively detecting the presence or absence in said individual of IgG antibodies immunoreactive with each of said immunoreactive BoNT/A peptide.

138. (New) The method of claim 12, wherein the presence or absence of antibodies immunoreactive with each of said immunoreactive BoNT/A peptide is detected using an enzyme-linked immunosorbent assay.

139. (New) The method of claim 12, wherein the presence or absence of antibodies immunoreactive with each of said immunoreactive BoNT/A peptide is detected using a radioimmunoassay.